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Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Non-fluoride caries preventive agents.

Bibliographic Source(s)

Rethman MP, BeltrÃ¡n-Aguilar ED, Billings RJ, Burne RA, Clark M, Donly KJ, Hujoel PP, Katz BP, Milgrom P, Sohn W, Stamm JW, Watson G, Wolff M, Wright JT, Zero D, Aravamudhan K, Frantsve-Hawley J, Meyer DM, American Dental Association Council on Scientific Affairs Expert Panel [trunc]. Non-fluoride caries preventive agents. Chicago (IL): American Dental Association; 2011 May 24. 56 p. [108 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The levels of certainty (high-low) and the grade of recommendations (strong-expert opinion) are defined at the end of the "Major Recommendations" field.

Clinical Considerations and Recommendations

A clinician must consider a patient's risk of experiencing disease and other factors such as readiness for change, oral health literacy and compliance when developing an optimal caries prevention plan. Patient education, dietary advice and periodic clinical examinations should be part of such a plan. Clinicians should encourage parents and caregivers to limit a child's consumption of sugar-containing foods and drinks and, when possible, to confine consumption to meal times.

In light of good supportive evidence the panel reminds clinicians that professional and home fluoride products, including fluoridated toothpastes and dental sealants remain the primary interventions effective in preventing caries and recommends that clinicians follow published evidence-based guidelines for these modalities. In contrast, the modalities examined in this review had less evidentiary support, both for and against.

Regarding some studies in which the evidence was lacking, of poor quality, or contradictory and the in which the panelists could not reliably estimate the benefit versus the basis of the findings of published studies, the panelists concluded that there was insufficient evidence. In such cases, clinicians and patients alike should understand fully the uncertainty in the underlying evidence as well as any potential risks of using or not using a particular intervention. The patient's caries risk status, the practitioner’s professional judgment, and a patient's needs and preferences should guide all decision-making.

The panel made recommendations for specific non-fluoride agents in Table 5 (see the original guideline document) based on the best available evidence and the balance between benefits and adverse events.

Recommendations from the American Dental Association Council on Scientific Affairs Non-fluoride Caries-Preventive Agents Expert Panel

This panel acknowledges the oral and systemic benefits of lowering the quantity and frequency of sugar consumption and encourages practitioners to provide dietary counseling. The panel also strongly recommends that practitioners first implement evidence-based recommendations regarding topical fluorides and sealants before attempting to use any non-fluoride therapies. The following recommendations may be considered as adjuncts to dietary counseling and a regular caries preventive program* offered to patients at higher risk for caries.

*A regular caries preventive program includes routine and periodic examination by a dentist, patient education, dietary advice and appropriate use of professional and home fluoride products and dental sealants.

Evidence-based Recommendations

- Advise parents and caregivers of children 5 years or older, that use of sucrose-free polyol (xylitol only or polyol combinations) chewing gum for 10-20 minutes after meals may reduce incidence of coronal caries. (Weak)
- Apply 1:1 mixture of chlorhexidine/thymol varnish every three months to reduce the incidence of root caries. (In favor)
- Applying 10 – 40 percent chlorhexidine varnish alone or in combination with fluoride for prevention of coronal caries is not recommended. (Against)
- Using 0.12 percent chlorhexidine rinse alone or in combination with fluoride for prevention of coronal or root caries is not recommended. (Against)
- Advise adults, that use of sucrose-free polyol (xylitol only or polyol combinations) chewing gum for 10 – 20 minutes after meals may reduce incidence of coronal caries. (Expert Opinion)
- Advise parents and caregivers of children 5 years or older, that the daily use of xylitol-containing lozenges or hard candy that are dissolved slowly in the mouth after meals may reduce incidence of coronal caries. (5-8 grams/day divided into two to three doses) (Expert Opinion)
- Applying 0.5 to 1.0 percent chlorhexidine gel alone or in combination with fluoride for caries prevention of coronal or root caries is not recommended. (Expert Opinion)
- Applying 1:1 mixture of chlorhexidine/thymol varnish alone or in combination with fluoride for prevention of coronal caries is not recommended. (Expert Opinion)

Definitions:

Definitions for Levels of Certainty*

Level of Certainty	Description
High	Strongly established by the best available evidence. The body of evidence usually includes consistent results from well-designed, well-conducted studies in representative populations. This conclusion is unlikely to be strongly affected by the results of future studies.
Moderate	Based on preliminary determination from the current best available evidence. But confidence in the estimate is constrained by one or more factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited applicability due to the populations of interest • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	Available evidence is insufficient to support the statement or the statement is based on extrapolation from the best available evidence

Level of Certainty	Description
	Evidence is insufficient or reliability of estimated effects is limited by factors such as: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies gaps in the chain of evidence • Findings not applicable to the populations of interest • A lack of information on important health outcomes More information may allow a reliable estimation of effects on health outcomes.

Definitions for the Strength of Recommendations*

Grade	Strength of Recommendation
Strong	Evidence strongly supports providing this intervention
In Favor	Evidence favors providing this intervention
Weak	Evidence suggests implementing this intervention after alternatives have been considered
Against	Evidence suggests not implementing this intervention or discontinuing ineffective procedures
Expert Opinion	Expert Opinion guides this recommendation

*Adapted from the United States Preventive Services Task Force (USPSTF) system.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Dental caries

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Prevention

Treatment

Clinical Specialty

Dentistry

Family Practice

Pediatrics

Preventive Medicine

Intended Users

Dentists

Public Health Departments

Guideline Objective(s)

- To present evidence-based clinical recommendations on non-fluoride caries preventive agents on the market in the United States
- To assist practitioners with decision-making about the use of non-fluoride caries preventive agents to arrest, prevent or reverse caries

Target Population

Adults and children with or at risk of dental caries

Interventions and Practices Considered

1. Sucrose-free polyol (xylitol or polyol combinations) chewing gum
2. Chlorhexidine/thymol varnish application
3. Xylitol containing lozenges or hard candy

Major Outcomes Considered

- Incidence of dental caries
- Side effects of non-fluoride agents

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search

One author used the following strategy to search MEDLINE through PubMed. She searched the Cochrane Library with a similar search strategy. She also searched references of selected articles in order to include studies that might have been missed through the electronic sources.

Search Terms: Dental Caries AND (prevention OR arrest OR reversal OR reduction OR incidence OR regression OR progression OR DMF Index[Mesh] OR ICDAS OR caries increment OR prevented fraction) AND ("casein phosphopeptide-amorphous calcium phosphate nanocomplex"[Substance Name] OR "amorphous calcium phosphate"[Substance Name] OR casein phosphopeptides OR calcium OR phosphate OR "Tooth Remineralization" OR "Tooth Demineralization" OR MI paste OR chewing gum OR "Sugar Alcohols"[Mesh] OR "artificial sweetener" OR chlorhexidine OR Thymol OR iodine OR triclosan OR cetylpyridinium chloride OR pilocarpine OR Salagen OR cevimeline)

Limits: Humans

The search of MEDLINE and the Cochrane Library from 1966 through April 9, 2010 identified 2697 articles. One author identified six additional publications by manual search. Two authors independently screened the articles using the inclusion and exclusion criteria presented in Table 1 in the original guideline document. Two members of the expert panel resolved disagreements between the reviewers.

While most of the inclusion and exclusion criteria were set apriori, the decision to exclude split-mouth studies and short-term (less than one years' duration) studies that reported only on white-spot-lesions was made after screening had begun. Split-mouth studies were excluded because of concerns regarding site isolation and longitudinal crossover effects. Short-term studies that only reported on white-spot lesions were excluded because short-term subtle outcome differences between test and control arms may provide misleading results when compared to long-term more clinically relevant outcomes. The guideline panel did not contact the authors of the included studies for baseline caries data when it was not reported in the published paper. Such studies were excluded because the panel could not characterize the baseline caries status of the population. For more information on Excluded Studies, see Appendix 2 of the original guideline document. See Table 1 in the original guideline document for details of the inclusion and exclusion criteria.

Search Update

Following the initial search on April 9, the search was periodically updated with the final update conducted on March 8, 2011. This update identified three additional articles for inclusion.

Number of Source Documents

The panel included 71 published articles whose authors described 50 randomized controlled trials (RCTs) and 15 non-randomized studies to assess the efficacy of various non-fluoride caries preventive agents.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions for Levels of Certainty*

Level of Certainty	Description
High	Strongly established by the best available evidence. The body of evidence usually includes consistent results from well-designed, well-conducted studies in representative populations. This conclusion is unlikely to be strongly affected by the results of future studies.
Moderate	Based on preliminary determination from the current best available evidence. But confidence in the estimate is constrained by one or more factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited applicability due to the populations of interest • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	Available evidence is insufficient to support the statement or the statement is based on extrapolation from the best available evidence Evidence is insufficient or reliability of estimated effects is limited by factors such as: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies gaps in the chain of evidence

Level of Certainty	Description
	• Findings not applicable to the populations of interest • A lack of information on important health outcomes
	More information may allow a reliable estimation of effects on health outcomes.

*Adapted from the United States Preventive Services Task Force (USPSTF) system.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Critical Appraisal of Included Studies

Based on a published review of critical appraisal instruments for randomized and non-randomized interventions, one author identified an instrument suitable to appraise randomized and non-randomized trials for this systematic review. The questions in the instrument addressed five separate domains including reporting, external validity, bias, confounding and statistical power. All panel members participated in an orientation through a conference call to standardize the application of the critical appraisal instrument. Along with a copy of the instrument, each panel member received five to six studies to review. Independent from the panel member, one author duplicated the review and critical appraisal across all included studies. This ensured appraisal by two independent reviewers and standardized application of the instrument by all reviewers. Following the critical appraisal, a composite score was developed for each study based on a standardized rating scale as follows.

Reporting (range 1 - 10) >9 = Good; 8 - 7 = Fair; <6 = Poor; Internal validity including bias, confounding and power (range 1 - 14) >12 = Good; 11 -10 = Fair; <9 = Poor.

During the panel meeting, all panel members reviewed and extensively discussed results from each study.

Data Synthesis and Meta-analysis

Choice of outcome measures. Caries increment was the outcome measure assessed for each study. Caries increment is the number of new decayed, missing or filled surfaces or teeth (DMF) experienced by each treatment group included in a study. The panel adapted a set of rules published in a recent Cochrane review of caries trials to select outcome data from each study for subsequent analysis. Specifically, the panel chose data on tooth surfaces level over data on tooth level; data for "all surface types combined" over data for "specific types" only; data for "all erupted and erupting teeth combined" over data for "erupted" only, and this over data for "erupting" only"; data from "clinical and radiological examinations combined" over data from "clinical" only, and this over "radiological" only; DMF surfaces (DMFS) scores over decayed, filled surfaces (DFS) or decayed surfaces (DS); data for "dentinal/cavitated" caries lesions over data for "all stages" over data for "enamel/non-cavitated" lesions; net caries increment data over crude (observed) increment data; and follow up nearest to three years (often the one at the end of the treatment period) over all other lengths of follow up. Further, the panel chose DMFS data over decayed, extracted, filled surfaces (defs) data unless otherwise stated.

Combining relevant treatment arms. For studies that evaluated more than one relevant treatment arm, we combined the raw results (the numbers, mean DMF increments and standard deviations) from all parallel arms in order to obtain an estimate of treatment effect.

Imputing variances. When possible, we imputed missing standard deviations that were not reported using linear regression of log (standard deviations) on log (mean caries) increments.

Summary estimate. When possible, meta-analysis was used to synthesize the results when multiple papers were included in the review. Meta-analyses use statistical methods to calculate a weighted average of the size of treatment effect when studies with the same outcome measure are combined. Similar to the summary estimate used in the Cochrane review of caries trials, the panel selected "prevented fraction" (PF) as the measure of treatment effect. PF is the difference in DMF increment scores between the groups that received the experimental treatment and those who received a comparison or no active treatment divided by the average number of DMF scores in people who received a comparison or no active treatment. Variances were estimated using a previously published formula. The summary estimate used for the meta-analysis was "prevented

fraction" that gives the reader an understanding of the relative preventive effect found between treatments. Since the "prevented fraction" is not based on standard epidemiological measures of risk and rate, it does not provide an estimate of the magnitude of treatment effect. Differences in outcome measures reported among studies precluded the panel from meaningfully combining the studies to estimate the magnitude of caries preventive effect.

Generating forest-plots. Random-effects meta-analyses were conducted throughout to generate forest plots using RevMan 5 software.

Heterogeneity. The I^2 statistic generated by RevMan quantified the statistical heterogeneity. The panel did not consider any formal methods to further investigate heterogeneity. The panel used a random-effects model to overcome some of the limitations of heterogeneous data and graded the level of certainty based on these considerations.

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

The authors are a multidisciplinary panel of subject matter experts convened by the American Dental Association (ADA) Council on Scientific Affairs (CSA).

The panel addressed two clinical questions:

1. In the general population, does the use of a non-fluoride caries preventive agent reduce incidence, arrest or reverse caries?
2. In individuals at higher caries risk, does the use of a non-fluoride caries preventive agent reduce incidence, arrest or reverse caries? (Trials that specifically enrolled subjects with incipient or cavitated lesions, prior caries experience or those with high salivary or plaque *Streptococcus Mutans* scores levels categorized as providing evidence for "high-risk" patients).

Process for Developing Clinical Recommendations

The panel developed evidence statements based on the body of evidence and graded the level of certainty of the evidence as high, moderate or low on the basis of a standardized grading system (see the "Rating Scheme for the Strength of the Evidence" field). Then, the panel developed clinical recommendations. When the panel found evidence supporting efficacy, the panel members assessed adverse events reported in the trials and discussed any potential adverse events that could be associated with the intervention based on their knowledge of the existing literature. (Note that the panel did not conduct a review of the data specifically for adverse effects). Based on the level of certainty and the magnitude of net benefit (see Table 3 of the original guideline document) the panel graded the strength of each (see the "Rating Scheme for the Strength of the Recommendations" field). When the panel was unable to reach a consensus in interpreting evidence into clinically relevant recommendations or when it made recommendations based largely on expert consensus, it used a simple majority vote to make final determinations.

Rating Scheme for the Strength of the Recommendations

Definitions for the Strength of Recommendations*

Grade	Strength of Recommendation
Strong	Evidence strongly supports providing this intervention
In Favor	Evidence favors providing this intervention
Weak	Evidence suggests implementing this intervention after alternatives have been considered
Against	Evidence suggests not implementing this intervention or discontinuing ineffective procedures
Expert Opinion	Expert Opinion guides this recommendation

*Adapted from the United States Preventive Services Task Force (USPSTF) system.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The panel sought comments to the original guideline document from other subject matter experts, methodologists, epidemiologists and end-users before finalizing the recommendations. The Council on Scientific Affairs (CSA) approved the final report for publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate use of non-fluoride caries preventive agents
- Decrease in dental caries

Potential Harms

- Chewing gum is considered a potential choking hazard and the American Academy of Pediatrics (AAP) recommends against gum chewing by children younger than 4 years old.
- Polyols in large doses have been linked to adverse gastrointestinal effects in some individuals.
- Hard candy should be used under supervised conditions in neurologically healthy children to reduce the risk of choking.

Qualifying Statements

Qualifying Statements

- The recommendations in this document do not purport to define a standard of care and rather should be integrated with a practitioner's professional judgment and a patient's needs and preferences.
- This report is intended to assist practitioners with decision-making about the use of non-fluoride caries preventive agents to arrest, prevent or reverse caries. The recommendations in this document are not intended to define a standard of care and rather should be integrated with a practitioner's professional judgment and a patient's needs and preferences.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Rethman MP, BeltrÃ¡n-Aguilar ED, Billings RJ, Burne RA, Clark M, Donly KJ, Hujoel PP, Katz BP, Milgrom P, Sohn W, Stamm JW, Watson G, Wolff M, Wright JT, Zero D, Aravamudhan K, Frantsve-Hawley J, Meyer DM, American Dental Association Council on Scientific Affairs Expert Panel [trunc]. Non-fluoride caries preventive agents. Chicago (IL): American Dental Association; 2011 May 24. 56 p. [108 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 May 24

Guideline Developer(s)

American Dental Association - Professional Association

Source(s) of Funding

- American Dental Association
- Centers for Disease Control and Prevention

Guideline Committee

American Dental Association (ADA) Council on Scientific Affairs Expert Panel on Non-fluoride Caries Preventive Agents

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Financial Disclosures/Conflicts of Interest

Drs. Burne and Rethman are consultants for Colgate, New York City. Dr. Donly has received financial research support from BISCO, Schaumburg, Ill.; Church and Dwight, Princeton, NJ; Dentsply, York, PA; the Health Resources and Services Administration, Rockville, MD; Ivoclar Vivadent, Schaan, Liechtenstein; the National Institute of Dental and Craniofacial Research, Bethesda, MD; 3M ESPE, St. Paul, MN; Oral B, Cincinnati; Philips, Andover, MA; and Procter & Gamble, Cincinnati, OH. Dr. Milgrom is the scientific director of ADP Silver Dental Arrest, Redmond, OR; is a member of the Cadbury Global Oral Health Advisory Committee, Parsippany, NJ; and is a consultant for the U.S. Food and Drug Administration, Silver Spring, MD. Dr. Zero consults with and conducts studies for GlaxoSmithKline, Research Triangle Park, NC; Johnson & Johnson, New Brunswick, NJ; Procter & Gamble; and Wrigley, Chicago, IL. None of the other authors reported any disclosures.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the American Dental Association Web site .

Print copies: Available from the American Dental Association, 211 E. Chicago Avenue, Chicago, IL 60611.

Availability of Companion Documents

The following are available:

- Non-fluoride caries preventive agents. Executive summary of evidence-based clinical recommendations. A report of the American Dental Association (ADA) Council on Scientific Affairs; 2011. 8p. Electronic copies: Available in Portable Document Format (PDF) from the American Dental Association (ADA) Web site .
- Non-fluoride caries preventive agents: evidence-based clinical recommendations. Chair-side guide. American Dental Association Council on Scientific Affairs; 2011. 2 p. Electronic copies: available in PDF from the ADA Web site .
- Non-fluoride caries preventive agents: evidence-based clinical recommendations. Podcast. American Dental Association Council on Scientific Affairs; 2011. Electronic copies: Available from the ADA Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 14, 2013. The information was verified by the guideline developer on March 19, 2013.

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